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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Nava Zisapel

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WASHINGTON, DC 20005

EXAMINER

CLARK, SARA E

ART UNIT

PAPER NUMBER

1612

NOTIFICATION DATE

DELIVERY MODE

04/01/2010

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No. 10/510,625	Applicant(s) ZISAPEL, NAVA	
	Examiner SARA E. CLARK	Art Unit 1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 October 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 29-37, 48 and 49 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 29-37, 48 and 49 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10/16/2009</u> . | 6) <input type="checkbox"/> Other: _____ |

FINAL REJECTION

Receipt is acknowledged of Applicants' Amendments and Remarks, filed 10/16/2009.

Claims 1-28 and 38-47 have been cancelled.

Claims 29, 31, and 32 have been amended and incorporate no new matter.

New claims 48 and 49 have been added.

Thus, claims 29-37, 48, and 49 now represent all claims currently pending and under consideration.

INFORMATION DISCLOSURE STATEMENT

The information disclosure statement (IDS) submitted on 10/16/2009 was filed after the mailing date of the Office Action on 4/17/2009. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

WITHDRAWN REJECTIONS

Rejections under 35 USC §102(b)

Due to the amendments to the claims, the rejection of claims 29 and 34-37 under 35 USC 102(b) as anticipated by **Bersani** has been withdrawn.

Due to the amendments to the claims, the rejection of claims 29 and 34-37 under 35 USC 102(b) as anticipated by **Suhner** has been withdrawn

MAINTAINED REJECTIONS

The following rejections are maintained from the previous Office Action dated 4/17/2009, on the ground that the references cited therein continue to read on the limitations of the amended claims.

Rejections under 35 USC §103(a)

Claims 30 and 31 stand rejected under 35 USC 103 as obvious over Suhner in view of Ohkawa. In addition, **this rejection is extended to amended claims 29 and 34-37, and new claims 48 and 49.** See below.

Claims 32 and 33 stand rejected under 35 USC 103(a) as obvious over Suhner and Ohkawa, further in view of Richardson.

Claims 29-31 and 34-37 stand rejected under 35 USC 103(a) as obvious over Ohkawa. In addition, **this rejection is extended to new claims 48 and 49.** See below.

Claims 32 and 33 stand rejected under 35 USC 103(a) as obvious over Ohkawa, further in view of Richardson.

RESPONSE TO ARGUMENTS

Applicant's arguments filed 10/16/2009 have been fully considered but they are not persuasive. Specifically, Applicant contends that the cited references do not teach or suggest all the elements of the amended claims.

With respect to **Suhner**, Applicant contends that the reference does not teach or suggest that the combination of melatonin and zolpidem are useful in decreasing sleep latency; that is, reducing the period of time until sleep onset, which corresponds to "promoting sleep initiation" as recited by the amended claims (Remarks, p. 7). However, Applicant goes on to note that Suhner shows that the combination of melatonin and zolpidem improved sleep latency (over melatonin alone and zolpidem alone) only on the third night of a four-night course of treatment of subjects recovering from eastward-travel jet lag (Table II), reproduced in relevant part here:

Sleep latency (min)	Night 1	Night 2	Night 3	Night 4	Baseline
Melatonin	12.9 ± 18.0	30.8 ± 44.2	28.7 ± 36.1	14.4 ± 20.1	11.5 ± 8.2
Zolpidem	9.0 ± 6.7	11.2 ± 9.9	19.3 ± 25.6	15.0 ± 19.4	10.6 ± 8.1
Melatonin + zolpidem	11.1 ± 13.8	23.7 ± 40.0	16.9 ± 32.6	15.0 ± 16.0	10.9 ± 5.3
Placebo	10.2 ± 10.2	25.8 ± 48.1	31.6 ± 54.0	17.3 ± 21.8	11.7 ± 8.1

Suhner thus explicitly discloses that the combination of melatonin and zolpidem is capable of reducing sleep latency/promoting sleep initiation (16.9 min) to a greater degree in comparison with melatonin alone (28.7 min) or with zolpidem alone (19.3 min). That the data demonstrates this on only one night out of four during the treatment of a specific sleep disorder (jet lag) is of no moment. The claims do not require the

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therapeutic effect (promotion of sleep initiation) to be maintained over any particular time interval or with respect to any particular sleep disorder.

Therefore, the only claim limitation Suhner does not disclose is melatonin in a sustained release form.

Applicant contends that **Ohkawa** does not remedy the deficiencies of Suhner, in particular that the skilled artisan "would come away only believing that stage 3 and stage 4 sleep can be affected" on the basis of the examples disclosed by Ohkawa (Remarks, p. 8-9), and would interpret the teachings of Ohkawa to affect *sleep quality* rather than *sleep initiation* (Remarks, p. 10), as recited by the amended claims.

However, this is an overly restrictive reading of the reference, as Ohkawa discloses methods of treating and/or preventing sleep disorders, such as primary insomnia, and sleep-awake rhythm disorders such as work-shift syndrome and jet lag (col. 4, lines 54-60) by administering a combination of compound A (a melatonin analog) and zolpidem in a single dosage form, wherein compound A is in a sustained release preparation (col. 4, lines 17-25). Therefore, Ohkawa remedies the deficiencies of Suhner.

Applicant contends that **Richardson** does not compensate for the shortcomings of the primary and secondary references, which alone or in combination do not suggest the claimed invention, but gives no specific reasons to support this assertion (Remarks, p. 9-10 and 10-11).

Finally, it is noted that the amended claims recite methods of promoting sleep initiation in a human who has difficulty falling asleep, by administering melatonin in a sustained release form in combination with zolpidem in a regular (immediate) release

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form. It follows that, upon administration of the claimed composition, zolpidem release to the systemic circulation occurs first, followed by delayed and/or sustained release of melatonin. Thus, zolpidem is the active ingredient primarily relied upon to promote sleep initiation, not melatonin, which in sustained release form would take longer to reach the circulation and exert its effects.

The comparative data disclosed by Suhner suggests the advantages of just such a formulation: Table I shows that in-flight sleep latency (time to sleep onset) is the shortest with zolpidem alone (13 min), followed by zolpidem + melatonin (20 min), melatonin alone (35 min), and placebo (38 min). These results correlate with subjects' reports of ease of falling asleep, on a scale of 0 (very difficult) to 4 (very easy), in which zolpidem ranked first at 2.9, followed by zolpidem + melatonin (2.5), melatonin alone (1.6), and placebo (1.2).

Because these results were achieved in-flight (that is, before jet lag set in), the data presented by Suhner directly suggests that zolpidem + melatonin would be useful to promote sleep initiation in any sleep disorder in which the time to reach sleep onset is problematic. Ohkawa reinforces this by disclosing the combination of zolpidem plus a melatonin analog in the treatment of primary insomnia (col. 4, lines 54-60), which, as evidenced by MedLine Plus, refers to insomnia that is not caused by any known physical or mental condition, and is characterized by difficulty falling asleep on most nights.

For these reasons, Ohkawa explicitly, implicitly, or inherently discloses all the limitations of the amended claims, alone or in combination with Suhner and/or Richardson, and therefore the foregoing rejections of record are maintained.

CONCLUSION

Claims 29-37, 48, and 49 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

CORRESPONDENCE

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SARA E. CLARK whose telephone number is (571) 270-7672. The examiner can normally be reached on Mon - Thu, 7:30 am - 5:00 pm (EST).

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass, can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SARA E. CLARK/
Examiner, Art Unit 1612

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612